

ADME NTP Study S0093 Furfural

Sex/Species: adult male F344 rats.

Vehicle: oral, corn oil.

CASRN 98-01-1

Radiolabeled with carbon-14 in the carbonyl moiety; Furfural, [carbonyl-¹⁴C]

Studies Groups:

- Single 0.127 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.
- Single 1.15 mg/kg oral gavage to rats with sacrifice 72 hours postdose.
- Single 12.5 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.

A parallel study in F344 rats for furfuryl alcohol was done with 0.275, 2.75, and 27.5 mg/kg administered p.o. Comparison disposition data is shown here.

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TABLE 1

Urinary excretion of ^{14}C -radioactivity by male Fischer-344 rats after oral administration of ^{14}C -furfural

Time (hr)	Dose (mg/kg)		
	0.127	1.15	12.5
	Mean \pm SD Dose Excreted (%) ^a		
0-4	49.0 ^b	26.3 \pm 27.7	28.8 \pm 17.9
4-8	37.8 \pm 33.0	40.7 \pm 30.8	32.6 \pm 18.0
8-24	19.2 \pm 7.6	15.3 \pm 4.1	18.0 \pm 3.4
24-48	3.6 \pm 1.1	2.5 \pm 0.9	2.3 \pm 0.6
48-72	0.9 \pm 0.7	0.8 \pm 0.2	0.9 \pm 0.5
	Mean \pm SD Dose Excreted (Cumulative %) ^a		
0-4	49.0 ^b	26.3 \pm 27.7	28.8 \pm 17.9
0-8	62.3 \pm 10.2	67.0 \pm 5.1	61.4 \pm 8.2
0-24	81.5 \pm 3.0	82.2 \pm 2.5	79.3 \pm 5.4
0-48	85.1 \pm 2.0	84.7 \pm 2.4	81.6 \pm 5.3
0-72	86.0 \pm 1.9	85.5 \pm 2.4	82.5 \pm 5.6

^a Mean of data from 4 rats except where indicated.

^b Mean of data from the 2 rats which urinated during this time interval.

TABLE 2

Fecal excretion of ¹⁴C-radioactivity by male Fischer-344 rats after oral administration of ¹⁴C-furfural

Time (hr)	Dose (mg/kg)		
	0.127	1.15	12.5
	Mean ± SD Dose Excreted (%) ^a		
0-4	0.28 ± 0.46	0.00 ± 0.01	0.02 ± 0.01
4-8	0.05 ^b	0.01 ± 0.01	0.04 ± 0.02
8-24	1.39 ± 0.25	1.22 ± 0.37	1.36 ± 0.27
24-48	0.35 ± 0.15	0.46 ± 0.17	0.52 ± 0.21
48-72	0.03 ± 0.06	0.07 ± 0.05	0.08 ± 0.02
	Mean ± SD Dose Excreted (Cumulative %) ^a		
0-4	0.28 ± 0.46	0.00 ± 0.01	0.02 ± 0.01
0-8	0.31 ± 0.43	0.01 ± 0.02	0.05 ± 0.04
0-24	1.63 ± 0.36	1.23 ± 0.38	1.41 ± 0.28
0-48	1.97 ± 0.40	1.69 ± 0.33	1.93 ± 0.10
0-72	2.00 ± 0.42	1.75 ± 0.33	2.00 ± 0.12

^a Mean of data from 3-4 rats except where indicated.

^b Mean of data from 2 rats which defecated during this time interval.

TABLE 3

Exhalation of ¹⁴C-carbon dioxide by male Fischer-344 rats after administration of ¹⁴C-furfural at 12.5 mg/kg p.o.

Time (hr)	Rat			Mean ^a
	463	464	465	
	Dose Excreted (%)			
0-4	3.16	2.25	2.64	2.90
4-8	1.94	1.49	2.11	2.03
8-25	1.30	0.77 ^b	1.88	1.59
25-42	- ^c		0.20	0.10 ^d
	Dose Excreted (Cumulative %)			
0-4	3.16	2.25	2.64	2.90
0-8	5.10	3.74	4.75	4.93
0-25	6.40	4.51 ^e	6.54	6.47
0-42	6.40		6.74	6.57

^a Data from rat 464 was excluded from the mean because a portion of the dose entered the lung and resulted in fatal lung damage.

^b This value represents a time interval of 8-18 hr. Rat 464 was found dead at 18 hr.

^c Radioactivity in sample was less than twice background for the system.

^d For the purposes of calculating a mean the samples in which the radioactivity was less than twice background for the system were considered to contain zero percentage of the dose.

^e This value represents a time interval of 0-18 hr. Rat 464 was found dead at 18 hr.

TABLE 4

Concentration of ^{14}C -furfural equivalents in tissues of male Fischer-344 rats at 72 hr after oral administration of ^{14}C -furfural

Tissue	Mean \pm SD Concentration (nmol/g) ^a		
	Dose (mg/kg)		
	0.127	1.15	12.5
Plasma	# ^b	#	0.50 \pm 0.04
Blood Cells	#	#	0.63 \pm 0.02
Liver	0.03 \pm 0.00	0.31 \pm 0.03	3.41 \pm 0.27
Kidney	0.04 \pm 0.01	0.34 \pm 0.05	3.22 \pm 0.24
Heart	#	#	1.23 \pm 0.12
Lung	#	#	1.72 \pm 0.05
Brain	#	#	0.36 \pm 0.03
Fat	#	#	2.19 \pm 0.46
Skeletal Muscle	#	#	0.66 \pm 0.10
Spleen	#	#	1.59 \pm 0.12
Thymus	#	#	2.29 \pm 0.03

^a Mean of data from 4 rats.

^b Mean \pm SD not calculable because ^{14}C -radioactivity in all samples was less than twice background for the system.

TABLE 5

Percentage of the dose of ¹⁴C-radioactivity in tissues of male
Fischer-344 rats at 72 hr after oral administration
of ¹⁴C-furfural

Mean ± SD Fraction of Dose (%)^{a,b}

Tissue	Dose (mg/kg)		
	0.127	1.15	12.5
Plasma	# ^c	#	0.02 ± 0.01
Blood Cells	#	#	0.02 ± 0.00
Liver	0.11 ± 0.01	0.11 ± 0.01	0.11 ± 0.01
Kidney	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.00
Heart	#	#	<0.01
Lung	#	#	0.01 ± 0.00
Brain	#	#	<0.01
Fat	#	#	0.17 ± 0.03
Skeletal Muscle	#	#	0.26 ± 0.04
Spleen	#	#	<0.01
Thymus	#	#	<0.01
Total	0.13 ± 0.02	0.14 ± 0.01	0.61 ± 0.08

^a Percentages were calculated from the organ weights and by assuming that plasma = 3.75%, blood cells = 3.75%, fat = 9.50% and skeletal muscle = 47.5% of body weight.

^b Mean of data from 4 rats.

^c Mean ± SD not calculable because radioactivity in all samples was less than twice background for the system.

TABLE 6

Recovery of ¹⁴C-radioactivity after oral administration
of ¹⁴C-furfural to male Fischer-344 rats

Sample ^b	Mean ± SD Dose Recovered (%) ^a		
	Dose (mg/kg)		
	0.127	1.15	12.5
Urine	86.0 ± 1.9	85.5 ± 2.4	82.5 ± 5.6
Feces	2.0 ± 0.4	1.8 ± 0.3	2.0 ± 0.1
Cage Rinse	2.2 ± 1.6	2.4 ± 0.6	4.7 ± 3.0
Carbon Dioxide	** ^c	**	6.6 ^d
Tissues	0.1 ± 0.1	0.1 ± 0.1	0.6 ± 0.1
Total	90.3 ± 0.9	89.8 ± 2.4	89.9 ± 2.7 ^e 96.5 ^f

^a Mean of data from 4 rats except where indicated.

^b Carbon dioxide was collected up to 42 hr. Urine and feces were collected up to the time of sacrifice, at 72 hr. At sacrifice tissues and cage rinse were collected.

^c Carbon dioxide was not collected from rats administered ¹⁴C-furfural at this dose level.

^d Mean of data from 2 rats.

^e Excluding carbon dioxide

^f Including carbon dioxide

TABLE 7

Comparative disposition and metabolism of furfuryl alcohol and furfural after oral administration of ¹⁴C-labeled compounds to male Fischer-344 rats

Parameter	Furfuryl Alcohol		Furfural	
	Fraction of Dose (Mean ± SD %)			
	Dose (mg/kg)			
	0.275	27.5	0.127	12.5
Extent Absorption (minimum) ^a	88	87	86	83/89 ^b
Excreted Urine 0-72 hr	87.6 ± 3.4	86.7 ± 4.7	86.0 ± 1.9	82.5 ± 5.6
Excreted Feces 0-72 hr	3.6 ± 1.0	3.8 ± 0.2	2.0 ± 0.4	2.0 ± 0.1
Exhaled ¹⁴ CO ₂ 0-42 hr	** ^c	**	**	6.6
Tissues at 72 hr	0.5 ± 0.1	0.5 ± 0.1	0.1 ± 0.1	0.6 ± 0.1
Total Recovery by 72 hr	94.0 ± 1.9	94.4 ± 5.3	90.3 ± 0.9	89.9 ± 2.7 ^d /96.5 ^e
Excreted Urine 0-72 hr as:				
Furoic Acid	5.4	5.5 ± 0.7	0.7 ± 0.3	1.2 ± 0.2
Furoylglycine	78.8	73.2 ± 5.9	80.4 ± 2.7	76.3 ± 4.6
Furanacrylic Acid	6.3	7.9 ± 2.2	3.3 ± 0.7	4.4 ± 1.5

^a Equal to dose excreted in urine in 0-72 hr.

^b Equal to dose excreted in urine in 0-72 hr plus dose exhaled as ¹⁴CO₂ in 0-42 hr.

^c Not determined.

^d Excluding exhaled ¹⁴C-carbon dioxide.

^e Including exhaled ¹⁴C-carbon dioxide.